

# Thrombocytopenia

Scott Akin, MD

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# Objectives

- Define thrombocytopenia
- Review causes
  - Increased destruction
  - Decreased production
  - Other
- Outline workup
- Treatment
  - To transfuse or not?

# Thrombocytopenia

- Definition: platelets  $< 150,000$
- Normal platelets 150,000 - 450,000 (our lab 130-400)
- 2.5% of the normal population will have platelet count lower than “normal” which is NOT abnormal
- Platelets can fall by half, and still be in normal range...which is NOT NORMAL
- Platelets live for 8-10 days
- Younger platelets are larger and work better

# Causes of Thrombocytopenia:

## Decreased Production

Marrow suppression (usually pancytopenic):

- Post viral: parvo, Hep B/C, EBV, varicella, measles, mumps, rubella, MMR vaccine, CMV, toxo, mono, influenza
- Sepsis
- Aplastic anemia
- Direct megakaryocyte damage: HIV
- Direct toxicity to bone marrow: XRT, chemo, alcohol
- Marrow infiltration: lymphoma, Myelofibrosis, mets, TB
- Meds with toxic effect: (non immune mediated)
  - Thiazides, estrogens, sepra, chemo, cimetidine, famotidine

# Decreased Production

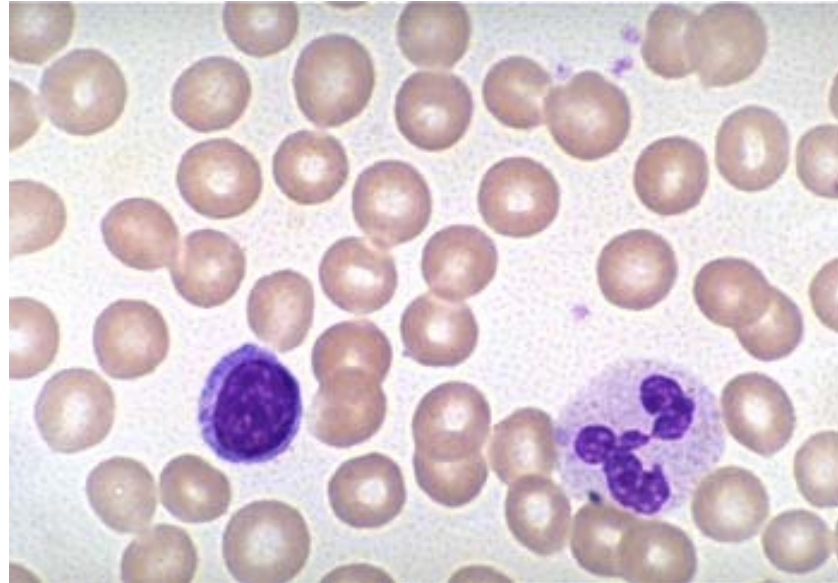
## (Continued)

- Malignancies: Myelodysplasia syndrome (age >60...usually anemic/leukopenic), leukemia, myeloma
- B12 or Folate deficiency (rare)
- Congenital (Wiskott-Aldrich, Fanconi syndrome, Bernard-Soulier)
- PNH

# Causes: Increased Destruction

- Immune mediated
  - ITP\*\*
  - Drug induced\*\*
  - Rheum: SLE, RA, APLA syndrome
  - HIV (40% of pts)
  - Post transfusion
  - Post transplantation
- Non-immune
  - TTP/HUS (suspect when low platelets and MAHA)
  - DIC
  - Pre-eclampsia
  - HELLP
  - Toxic shock
  - Vasculitis

# What's this?





# Increased Destruction: ITP

## (Idiopathic thrombocytopenic purpura)

- Diagnosis of exclusion with:
  - Isolated thrombocytopenia      -history of no possible offending meds
  - normal smear
  - Normal spleen size
- No gold standard for diagnosis
- Consider HIV test if risk factors
- Consider bone marrow biopsy if age >60 to rule out MDS
- Anti-platelet antibody panel not generally recommended (low sensitivity and specificity)

# Treatment of ITP

- If platelets  $> 20,000$  and no bleeding...generally observe
- Steroids, benefit approx 2/3 of patients...but takes 3 weeks
- IVIG works more quickly (several days, and lasts several weeks)...used generally in actively bleeding patients while waiting for steroids to work
- Immunosuppressive agents/splenectomy

# Medication induced Thrombocytopenia



# Increased Destruction: MEDICATIONS!!

- Mechanism of med → thrombocytopenia is accelerated plt destruction via drug dep antibody
- Don't forget about OTC meds, remedies
  - ASA, NSAIDS
  - Quinine (tonic water)
- Many, many meds can cause thrombocytopenia...and list constantly growing
- Median recovery after d/c of med is 5-7 days
- If plts <10,000 or bleeding...transfuse (class 1B rec)

# Medications

## The Main Offenders

**Heparin\*\***

**Valproic acid/Carbamazepine**

**Gold salts**

**Quinine/quinidine**

**Bactrim/sulfonamides**

**Penicillin/Beta lactams**

**Interferon**

**GP 2b/3a inhibitors (abciximab)**

**Linezolid**

Amiodarone

Amphotericin B

Vancomycin

Cimetidine

Phenytoin

Clopidogril

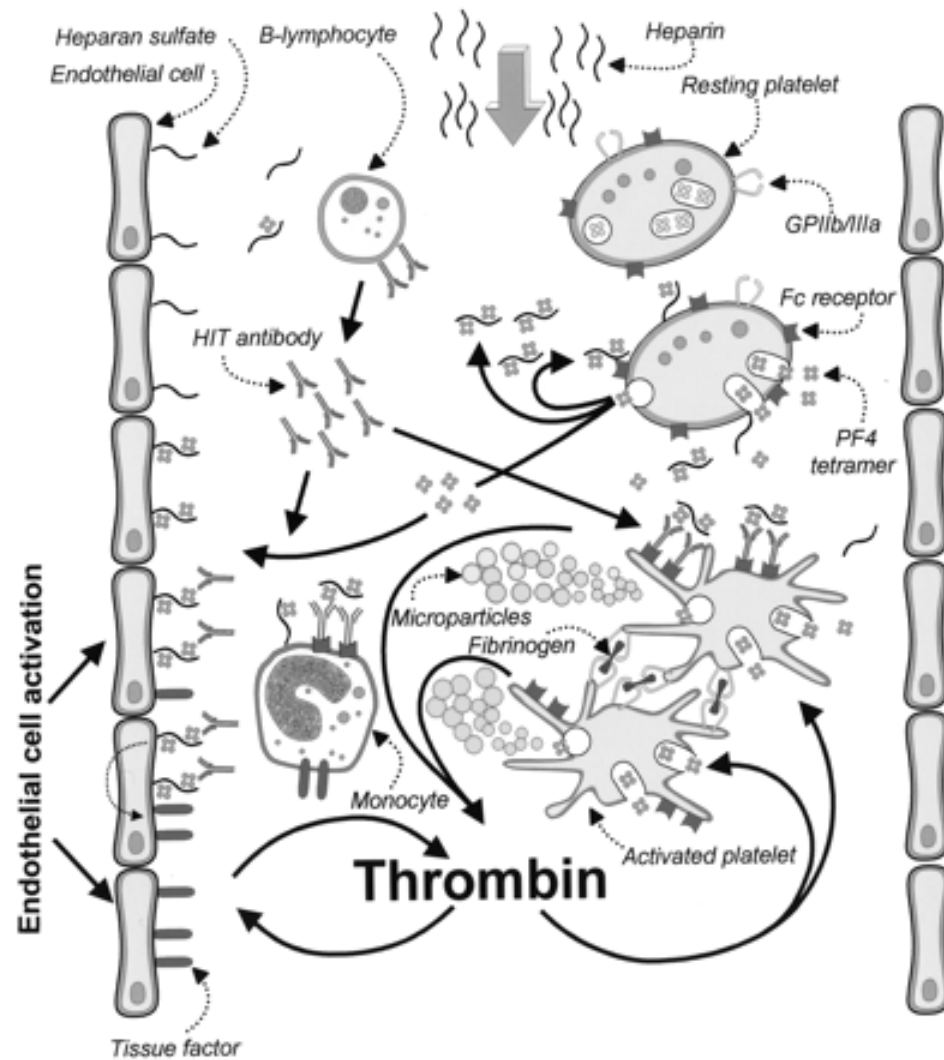
Digoxin

Fluconazole

Ranitidine

# HIT: Heparin induced thrombocytopenia

- Also referred to as Heparin induced thrombocytopenia *and thrombosis* (“HITT”)
  - Two types:
    - » HIT 1: Minimal fall of platelets within 2 days of heparin, then returns to normal...non-immune, not clinically important
    - » HIT II: immune mediated fall of platelets generally occurring within 5-10 days after heparin
- Can be associated with minimal use of heparin (even with IV flushes...why we now use saline)



# HIT

- Incidence: 0.2-5% of patients exposed to Heparin
- Factors predisposing one to HIT:
  - Longer duration of Heparin
  - Use of UFH (rather than LMWH/lovenox)
  - Surgical patient > medical patient
  - Female > male



# HIT

- When to suspect:
  - Patient on heparin, started  $>5$  days prior (or less if re-exposed to heparin)
  - 50% fall or more from a prior value (even if still within normal range)
  - Associated thrombosis (venous or arterial)
  - Associated skin necrosis at site of heparin injection

# HIT

- OK, you suspect it...now calculate a pretest probability: The 4 Ts
  - Thrombocytopenia
    - >50% fall and nadir >20K: 2 points
    - 30-50% fall or nadir 10-19K: 1 point
    - < 30% or nadir < 10K: 0 points
  - Timing
    - Clear onset between day 5-10 post heparin (or w/in 1 day if heparin previously w/in 30days): 2 points
    - “consistent with” between 5-10 days, but missing data: 1 point
    - Platelet fall < 4 days post heparin: 0 points

# HIT

- The next two Ts
  - Thrombosis:
    - NEW Thrombosis/necrosis/systemic reaction (after IV bolus): 2 points
    - Progressive/recurrent thrombosis, suspected thrombosis, or non-necrotizing skin lesions: 1 point
    - None of above: 0 points
  - Other causes for Thrombocytopenia
    - None: 2 points
    - Possible: 1 point
    - Definite: 0 points

# HIT

- \*0-3 points= low probability (0.9% pre-test probability) Evaluate for other causes, don't order HIT antibodies
- \*4-5 points= intermediate (11% pre-test prob)  
Stop heparin, order HIT antibodies
- \*6-8 points= high probability (34% pre-test prob)  
stop heparin, order HIT antibodies

# HIT Treatment

- Stop heparin.
- Stop warfarin pending rebound of platelet count (give vitamin K if warfarin already started).
- Consider checking for lower extremity DVTs.
- DON'T transfuse for prevention of bleeding (may precipitate thrombosis)...but consider in patients who “are bleeding or are deemed to be at high risk of bleeding.” (2008 ACCP guidelines).
- Start nonheparin anticoagulant if HIT antibodies positive (take 2-3 days).

# HIT Treatment

- Use nonheparin anticoagulant.
  - Lepirudin, argatroban, danaparoid, fondaparinux, bivalirudin.
  - If abnormal renal fxn: Argatroban (or lepirudin at reduced dose).
  - If abnormal hepatic function: lepirudin, danaparoid, fondaparinux.
  - If both: Argatroban, or reduced dose bivalirudin.
- Anticoagulation (with warfarin) for 2-3 months if no thrombotic event, 3-6 months if thrombotic event (grade 2C evidence)

# 2 More Causes of thrombocytopenia

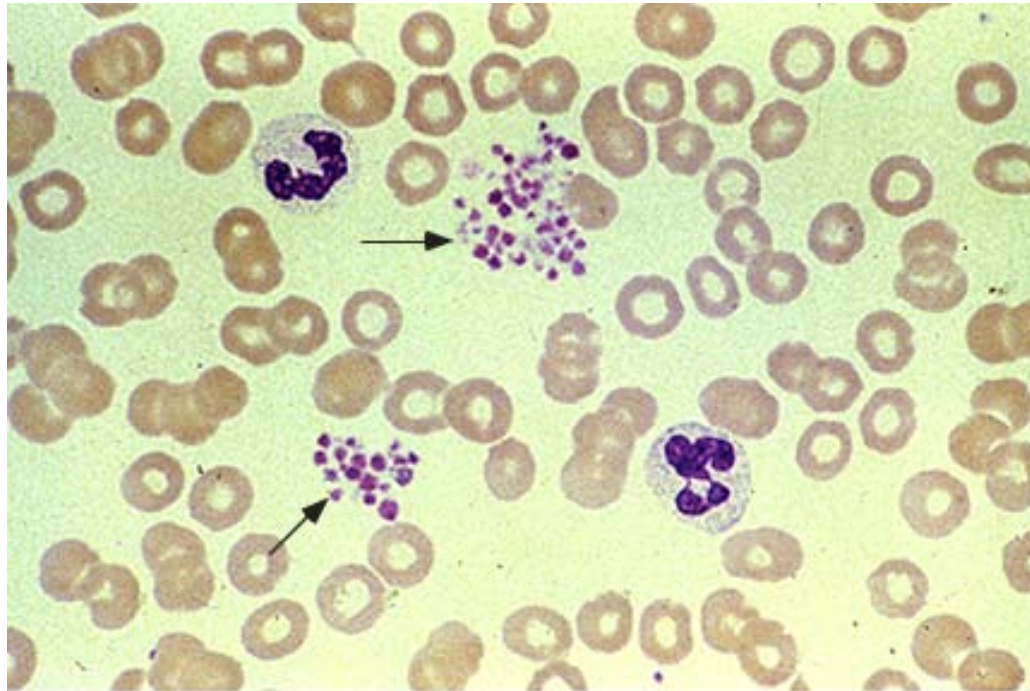


## 2 More Causes of thrombocytopenia

- Dilutional
  - Massive blood loss with transfusion (few platelets in PRBCs).
- Distributional
  - Normally 1/3 of platelets are sequestered in spleen.
  - With portal HTN→congestive splenomegaly→increased sequestration (up to 90%) in spleen→ low plt count in peripheral blood (but available platelet mass normal, therefore rarely bleed).  
Note that platelet count usually in 50-100K range.



A VERY common cause of  
“thrombocytopenia”



# Work up

- First rule out pseudothrombocytopenia  
(EDTA agglutinin autoantibody mediated Platelet clumping seen in 0.1%-0.2% of all blood draws)
  - \*Examine the smear
  - \*Repeat with heparinized/citrated tube
  - \*Repeat with fingerstick directly applied to slide
  - \*Note: pseudothrombocytopenia often accompanied by falsely high WBC (machine counts plt clumps as WBCs)

# Work up

- History
  - Meds, meds meds
  - Alcohol
  - Nutrition
  - Travel
  - HIV risk factors
  - “B” symptom assessment (? Occult malignancy)
  - Bleeding history (gums, menses, surgical complications).
  - Family History
- Physical
  - Examine spleen
  - Detailed skin exam, looking for
    - Petechiae: Red pinheads
    - Purpura: Purple confluent petechaie
    - ecchymoses
  - Look for lymphadenopathy



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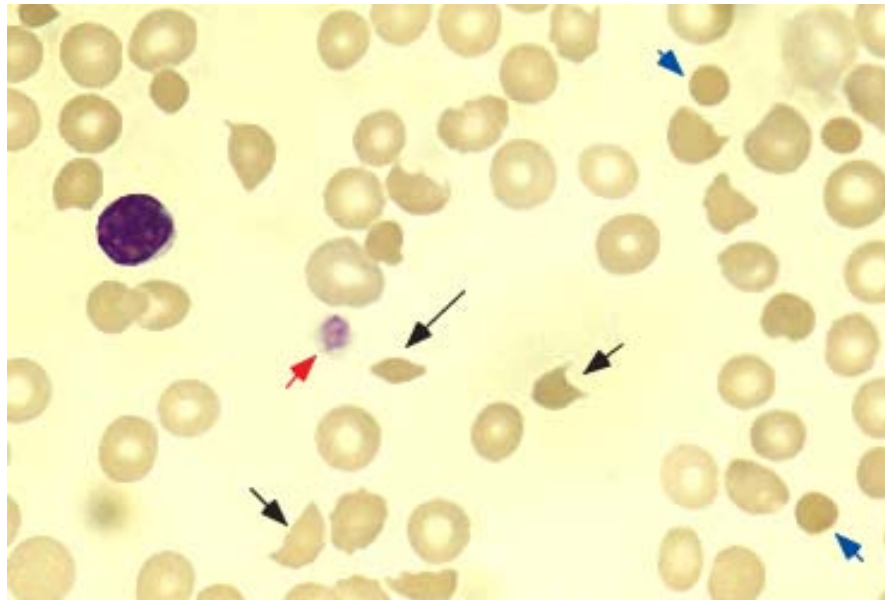
UBC Dermatology <http://www.derm.ubc.ca>

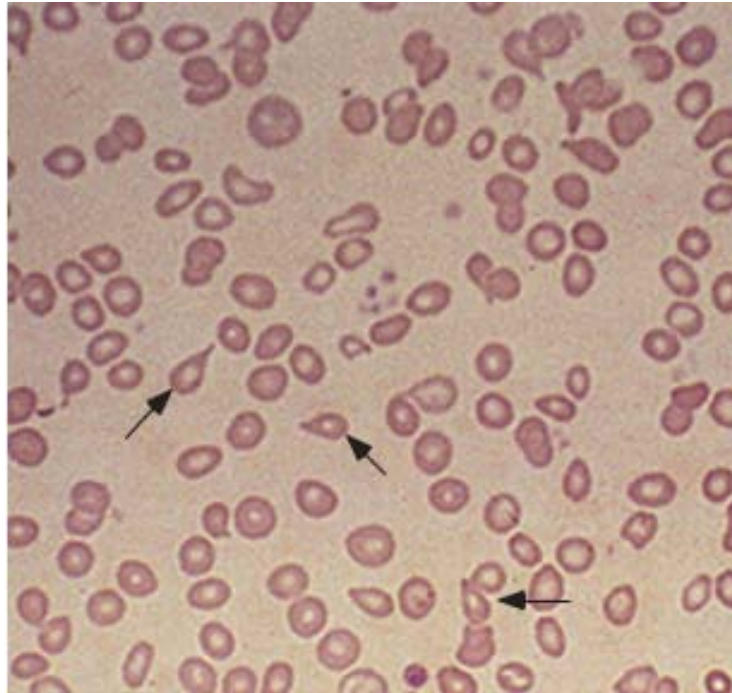


# Work up (Continued)

- Peripheral smear
  - large platelets (high MPV on CBC) imply increased destruction → early release from marrow (ITP)
  - Normal/small platelets suggest reduced BM response
  - Schistocytes (fragmented RBCs): MAHA
  - Can reveal blasts
  - Teardrop RBC, nucleated RBCs can suggest marrow invasion (tumor/fibrosis/granuloma)
  - Macrocytosis with hypersegmented polys can suggest Vitamin B/folate deficiency

# Diagnosis?







# Work up (Continued)

- PT/PTT (high in MAHA/DIC...liver disease)
- LDH (hemolysis/MAHA)
- Bun/Creatinine (HUS/TTP)
- Consider HIV, ANA if clinical suspicion
- Consider toxo, EBV, CMV serologies if lymphadenopathy, splenomegaly, or “B” symptoms
- Consider HIV(initial disease manifestation in 10%)
- Consider ANA if clinical suspicion

# Work up (continued)

- Bone marrow biopsy?
  - More definitively answers the “production vs. destruction” question
  - Generally indicated in unexplained thrombocytopenia if platelet count low enough (5-10K) to be at risk for major bleeding...
    - \*UNLESS age < 60, thrombocytopenia is isolated, and history/PE, and smear suggest the diagnosis (of exclusion) of ITP.
    - \*If age > 60, and suspect likely ITP, BM biopsy generally indicated to r/o myelodysplasia

# What platelet level is “safe” ??

- Plts > 50K: surgery safe (except neurosurg)
- Plts 30-50K: risk of major bleeding low.  
Rarely have purpura.
- Plts 10-30K: risk of mild-moderate bleeding (especially with more extensive trauma).
- Plts <10K: high risk for spontaneous hemorrhage (esp if <5K). These patients have spontaneous bruising, and maybe petechiae...
  - Avoid IM injections, rectal exams, enemas



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Taken : 17-FEB-04

Expres : 22-FEB-04

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24 Antigen, HTLV 1&2

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# When NOT to transfuse platelets

- Transfusions may induce immune resistance
- Generally transfusions not given in conditions of platelet destruction:
  - HUS/TTP
  - APLA unless severe
  - HIT CNS bleed or
  - DIC urgent invasive
  - Severe ITP procedure required

# When TO transfuse platelets

- If platelets  $< 10,000$  (risk of spont. Bleeding)
- If  $< 20,000$  and active bleeding
- If  $< 40-50,000$  prior to an invasive procedure
  - Surgery
    - Childbirth
  - Central line
    - Tooth extraction
  - Thoracentesis
- If  $< 100,000$  prior to neurosurgery/epidural anesthesia
- 1 “unit” of platelets (“phoresed unit”) raises platelet count by about 20,000

# Conclusion

- Think about thrombocytopenia in terms of etiology (destruction, decreased production, and “other”)
- History (especially MEDS) essential
- Always rule out psuedo-thrombocytopenia
- Peripheral smear tells you a lot
- Think before you transfuse

The end...

